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**Date:** 10/17/96  
**Subject:** Phthalic Anhydride Meeting

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On October 17, 1996, 1:30-2:20 pm industry and EPA held a teleconference on the "Alternative PK testing proposal for phthalic anhydride" prepared by industry. Industry had requested this meeting with ORD scientists in order to get feedback from EPA on whether their approach was on the mark before developing a full proposal and to allow the opportunity for EPA scientists to ask questions about their preliminary proposal.

The participants were: Annie Jarabek (ORD/NCEA/EPA), Daniel Costa (ORD/NHEERL/EPA), Vicki Dellarco (ORD/NCEA/EPA), Gary Timm (OPPT/EPA), Andrej Nikiforov (Exxon), Mike Gill (Phthalic Anhydride Task Group)

Summary of key points discussed:

1. Respiratory Sensitization-Annie Jarabek will follow up with Mary Jane Selgrade (ORD/NHEERL/EPA) on immunological approaches for evaluating respiratory sensitizers and will call Nikiforov/Gill with additional guidance.
2. Single Exposure Study-Two issues were raised by EPA -inclusion of bronchoalveolar lavage analysis as an early and sensitive indicator of pulmonary toxicity; and consideration of adding a longer duration of exposure in addition to the 4 hour duration to determine the CXT relationship. Nikiforov/Gill will take these issues back to the PA task group.
3. PK studies--EPA raised the issue of whether there was a kinetic aspect to the proposal and whether blood concentrations would be sufficient to characterize disposition. Industry acknowledged that it may be important to characterize the time course and account for mass balance by adding excretion data.
4. Consideration of exposure levels- Industry was considering a combination of vapor and aerosol exposure. EPA stated that industry should consider mixed vapor/dust exposure for the high concentration and vapor only exposure for the low concentration of the blood level study. This distinction was made because bioavailability could decrease with particle/needle exposure. Industry offered to try the vapor generation method; it was the only successful method noted in an industry sponsored study of test atmosphere generation methods. Industry acknowledged that composition of the test atmosphere may be more important than concentration in their study design and will consider the issue.
5. Systemic effects on the immune system: EPA asked inquired what approach industry would take to evaluate immune function. Industry indicated they wanted to wait for the outcome of the SAP meeting on the test guidelines. EPA indicated that the Sheep RBC assay is important to consider in their approach.

In general, EPA thought that the industry proposal was good and taking the right directions

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